Remarks

Applicants request reconsideration. Claims 20-40 are pending and have been examined.

Applicants' amendment incorporates the suggested language of the Examiner into claims 37 and 38, and adds new claims 41-50. The new claims conform to subject matter that the PTO indicates is allowable. For example, each of claims 41-50 recite a cell or method the Examiner considers enabled at page 3 of Paper No. 16. The claims also recite elements, the antigenic peptide for example, that are not subject to the anticipation and obviousness rejections of Paper No. 16. Accordingly, no new search or examination is required to enter and consider the new claims.

Applicants respectfully submit that the new claims are allowable. Alternatively, they place the application in better form for appeal by clarifying issues for review.

The new claims are supported by the specification as a whole. In addition, the cells and compositions containing them as specifically described at, for example, page 8, lines 23-25, page 16, lines 19-22, and Example 4 at page 26. The peptides recited in the new claims are specifically described at, for example, page 9, lines 8-21, and in Example 2, at page 22, lines 15-17. The methods in the new claims are specifically described at, for example, page 8, line 26, through page 9, line 7. Furthermore, the original claims support the new claims. Accordingly, no new matter enters by the new claims or the amendments to the claims.

Applicants respectfully request entry of the new claims. Any fee required for the entry of the new claims can be taken from the undersigned's Deposit Account No. 50-1129.

The Rejection under 35 U.S.C. § 112, first paragraph (enablement)

Claims 34-40 stand rejected under 35 U.S.C. § 112, first paragraph, as the specification allegedly does not enable the scope of the subject matter claimed. Applicants respectfully disagree.

Applicants note that the PTO recognizes that the cells infected *in vitro* with a replication defective recombinant adenovirus encoding a tumor specific antigen and the methods of

preparing cytotoxic T cell precursors with said adenoviruses are enabled by the specification (*see* page 3 of Paper No. 16). The new claims reciting these cells and methods are therefore not subject to this rejection.

Applicants have previously addressed the PTO's argument that certain second signals are "required" for cells to activate a mature cytotoxic T cell (*see* Response filed June 22, 2000, specifically incorporated herein by reference). That response explained from at least a Bachman *et al.* document (of record) why the claims are enabled and why additional signals would not be required. In Paper No. 16, the PTO points to Figure 2 in the submitted excerpt of Paul (Fundamental Immunology). The PTO asserts that Figure 2 substantiates a requirement for either exogenously added IL-2 or GM-CSF, or the use of particular antigen presenting cells in order for one of skill in the art to consider applicants' assertions of enablement of the invention. However, after Figure 2, in the text at page 968, the Paul textbook explains that mechanisms other than the production of IL-2 by CD4+ cells is known to exist and support the activation of pre-CTL cells. Accordingly, for at least both these reasons, applicants respectfully submit that PTO's position is in error. The PTO has failed to substantiate a *prima facie* case of lack of enablement. Applicants respectfully request withdrawal of the rejection.

The PTO also argues that the specification lacks sufficient data showing the "therapeutic effect on tumors" for the claimed invention (*see* pages 5-7) and that the state of the art for gene therapy at the time of filing was unpredictable. Irrespective of whether or not the term "pharmaceutical" is used in the claims, applicants have addressed these concerns in the past by explaining that the case law does not require human clinical data or exhaustive efficacy data to demonstrate that an invention is patentable. Applicants respectfully submit that, as explained in the Response filed June 22, 2000, the proper standard for analysis is not being applied in this instance.

Furthermore, applicants previously submitted the Mincheff *et al.* patent documet (WO 00/18933). The PTO does not consider this document connected to the current case. However, applicants submitted Mincheff to demonstrate that the cited Verma, Marshall, and Orkin documents, and the arguments built around them, do not establish the level of predictability one of skill in the art understands. While "additional therapies" may be discussed in Mincheff (*see* page 7 of Paper No. 16), the document does discuss how administering vectors encoding an antigen have the type of predictable biological response applicants' assert in their specification.

For example, applicants assert (at page 5, lines 1-7) that the appropriate mouse model establishes the ability to raise lymphocytic response using the vectors and methods of the invention. Page 30 of the specification asserts even more by explaining the successful results on lympholytic activity demonstrated *in vivo*. Nothing the PTO has presented detracts from applicants' assertions, arguments, and evidence that a lymphocytic response can be produced using the claimed vectors, cells, and methods. That evidence sufficient to establish efficacy in a human clinical trial has not been specifically presented has no import to the analysis.

Applicants respectfully request withdrawal of the rejection.

Rejection under 35 U.S.C. § 112, Second Paragraph

The Examiner suggested replacing the term "preparing" with "generating" (*see* page 9 of Paper No. 16). While applicants believe this change is unnecessary, applicants have replaced claims 37 and 38 with amended versions.

Rejection Under 35 U.S.C. § 102(b) over Zhai

Claims 20-23, 29, and 35-36 stand rejected under 35 U.S.C. § 102(b) as allegedly unpatentable over the abstract of Zhai *et al.* Applicants respectfully disagree.

The PTO asserts that the Zhai abstract includes all that is needed for one of skill in the art to believe that an adenoviral vector and compositions containing them have been made and used in an enabling manner. However, applicants respectfully point out that applicants' specification includes substantially more information on how to make and use the claimed invention than provided by the Zhai abstract. Applicants have also presented *in vivo* evidence of their successful use at Example 5. Nothing in Zhai suggests that the *in vitro* experiments can be successfully used *in vivo* as applicants have demonstrated. Respectfully, applicants cannot understand how a short abstract can possibly be an enabling, anticipatory reference for the claimed invention, even with inherent teachings to support it, when applicants' specification is not considered enabled. Applicants respectfully request clarification of the PTO's stance on the enablement of this reference.

Applicants' respectfully submit that the PTO has failed to show how the Zhai reference can be an enabling reference for the claimed invention and that a *prima* facie case of anticipation has not been made.

Applicants also point out that the Zhai abstract fails to teach or disclose the cells and methods of new claims 41-50, reciting an adenovirus comprising a sequence encoding an antigenic peptide of a tumor specific protein. Thus, new claims 41-50 cannot be anticipated by Zhai.

Rejections Under 35 U.S.C. § 103

Claim 30 stands rejected over Zhai in view of Hadada. Applicants respectfully disagree.

As noted above, applicants maintain that Zhai cannot be an enabling reference to the claimed invention. Hadada merely adds the discussion of a canine adenovirus. This does not remedy the failure of Zhai to demonstrate a teaching or suggestion, coupled with an expectation of success, of the claimed invention. Furthermore, what motivation is there to combine the alleged vector of Zhai with Hadada's discussion to arrive at the claimed invention of claim 30.

For these reasons, applicants respectfully request reconsideration and withdrawal of this rejection.

Claims 31-33 stand rejected over Zhai in view of Chen and claims 24-28, 37, and 39 stand rejected over Toso in view of Zhai and Chen. Applicants respectfully disagree.

Applicants have above dealt with the Zhai document. Nothing in Chen remedies the deficiencies of Zhai.

Furthermore, the Toso document relates to a canarypox virus vector. The PTO has provided no basis from which one of skill in the art could generalize any result from the experiments with canarypox viral vectors to adenoviral or any other viral vectors.

Applicants respectfully submit that a *prima facie* case of obviousness has not been made.

If the Examiner believes that discussing the application with applicants' representatives might further prosecution, the undersigned would welcome the opportunity to do so.

No additional extension of time fees, requests for extension of time, or additional claim fees are believed to be necessary to enter and consider this paper. If, however, any extensions of time are required or any fees are due or petitions required in order to enter or consider this paper or keep this application pending, including fees for net addition of claims, applicants hereby request any extensions or petitions necessary and the Commissioner is hereby authorized to charge Deposit Account # 50-1129 for any fees.

Respectfully submitted,
WILEY REIN & FIELDING LLP

Date: July 8, 2002

By: _____
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Enclosure: Marked-up Version of
Amended Claims 37 and 38

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Marked-up Version of Replaced Claims 37 and 38

37. A method for [preparing] generating cytotoxic T cells specific for a [tumour] tumor antigen, the method comprising contacting a cytotoxic T cell precursor with a population of cells infected with an adenovirus according to claim 20.

38. A method for [preparing] generating cytotoxic T cells specific for a [tumour] tumor antigen, the method comprising administering to a patient an adenovirus according to claim 20.